Clinical trial results:
The RECONSTRUCT study
Reconstructing Disease Mechanisms in Asthma

Summary

EudraCT number	2016-003509-33
Trial protocol	DK
Global end of trial date	01 April 2019

Results information

Result version number	v1 (current)
This version publication date	02 April 2021
First version publication date	02 April 2021

Trial information

Trial identification

Sponsor protocol code	RECONSTRUCT

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Lungemedicinsk Forskningsenhed, Bispebjerg Hospital
Sponsor organisation address	Bispebjerg bakke 23, indgang 66, København NV, Denmark, 2400
Public contact	Lungemedicinsk Forskningsenhed, Lungemedicinsk Forskningsenhed, Bispebjerg Hospital, +45 60770127, morten.hvidtfeldt@regionh.dk
Scientific contact	Lungemedicinsk Forskningsenhed, Lungemedicinsk Forskningsenhed, Bispebjerg Hospital, +45 60770127, morten.hvidtfeldt@regionh.dk

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	17 March 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 April 2019
Global end of trial reached?	Yes
Global end of trial date	01 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the correlation between increase in ASM content of Na+, K+ pumps and reduction in airway hyperresponsiveness to mannitol after six weeks of daily inhalation of glucocorticoid, in patients with asthma and to describe differences in ASM content of Na+, K+ pumps among healthy subjects and patients with non-eosinophilic asthma (NEA) or eosinophilic asthma (EA) respectively.
Primary endpoint:

Protection of trial subjects:

Trial subjects were monitored closely once weekly by phone

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 60
Worldwide total number of subjects	60
EEA total number of subjects	60

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	60
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were recruited continuously

Pre-assignment

Screening details:

Non-smoking patients with asthma and airway hyperresponsiveness to mannitol not currently on inhaled corticosteroids.

Period 1

Period 1 title	Intervention
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Type 2 high asthma

Arm description:

Type 2 high asthma based on FeNO > 25 ppb

Arm type	Active comparator
Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	Spirocort
Pharmaceutical forms	Inhalation powder, pre-dispensed
Routes of administration	Inhalation use

Dosage and administration details:

1600 ug daily

Arm title	Type 2 low asthma

Arm description:

Type 2 low asthma based on FeNO < 25 ppb

Arm type	Active comparator
Investigational medicinal product name	Budesonide
Investigational medicinal product code	
Other name	Spirocort
Pharmaceutical forms	Inhalation powder, pre-dispensed
Routes of administration	Inhalation use

Dosage and administration details:

1600 ug daily

Number of subjects in period 1[1]	Type 2 high asthma	Type 2 low asthma
Started	25	25
Completed	25	21
Not completed	0	4
Consent withdrawn by subject	-	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: -

Period 2

Period 2 title	Healthy controls
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Healthy controls
Arm description: -	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 2[2]	Healthy controls
Started	10
Completed	10

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: -

Baseline characteristics

Reporting groups

Reporting group title	Intervention

Reporting group description: -

Reporting group values	Intervention	Total	
Number of subjects	50	50	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	24		
inter-quartile range (Q1-Q3)	20 to 28	-	
Gender categorical Units: Subjects			
Female	25	25	
Male	25	25	

Subject analysis sets

Subject analysis set title	Type 2 high asthma
Subject analysis set type	Full analysis

Subject analysis set description:

Type 2 high asthma with FeNO>25 ppb at baseline

Subject analysis set title	Type 2 low asthma
Subject analysis set type	Full analysis

Subject analysis set description:

Type 2 low asthma with FeNO<25 ppb at baseline

Reporting group values	Type 2 high asthma	Type 2 low asthma	
Number of subjects	25	25	
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			

Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
median	26	23	
inter-quartile range (Q1-Q3)	21 to 31	19 to 27	
Gender categorical Units: Subjects			
Female	11	14	
Male	14	11	

End points

End points reporting groups

Reporting group title	Type 2 high asthma
Reporting group description: Type 2 high asthma based on FeNO > 25 ppb	
Reporting group title	Type 2 low asthma
Reporting group description: Type 2 low asthma based on FeNO < 25 ppb	
Reporting group title	Healthy controls
Reporting group description: -	
Subject analysis set title	Type 2 high asthma
Subject analysis set type	Full analysis
Subject analysis set description: Type 2 high asthma with FeNO>25 ppb at baseline	
Subject analysis set title	Type 2 low asthma
Subject analysis set type	Full analysis
Subject analysis set description: Type 2 low asthma with FeNO<25 ppb at baseline	

Primary: Airway hyperresponsiveness

End point title	Airway hyperresponsiveness
End point description: Doubling dose of PD15 to mannitol	
End point type	Primary
End point timeframe: Before and after intervention	

End point values	Type 2 high asthma	Type 2 low asthma	Type 2 high asthma	Type 2 low asthma
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	25	21	25	21
Units: Doubling dose				
geometric mean (confidence interval 95%)	3.98 (2.49 to 6.38)	3.85 (2.51 to 5.91)	3.98 (2.49 to 6.38)	3.85 (2.51 to 5.91)

Statistical analyses

Statistical analysis title	Difference in change in AHR
Comparison groups	Type 2 high asthma v Type 2 low asthma

Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.92
Method	t-test, 2-sided

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
During study period	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19

Reporting groups	
Reporting group title	All patients

Reporting group description: -

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 46 (2.17%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
psychiatric admission			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 46 (2.17%)		
Immune system disorders			
Asthma exacerbation, mild			
subjects affected / exposed	1 / 46 (2.17%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported